Please amend claims 17, 18, 19, 21, 22, 24, 28, 29, and 32 as indicated in the "mark-up" copy found in Appendix 2 of this Preliminary Amendment. A "clean" copy of the amended claims, in compliance with 37 C.F.R. §1.121, is found in Appendix 3 of this Preliminary Amendment.

REMARKS

The Specification has been amended at page 1, lines 4-7, to replace the existing paragraph with a new paragraph. A "clean" copy of the amendment to the Specification is found in Appendix 1. The Specification has been amended to insert a claim to priority to the parent application of this Divisional application and to remove reference to U.S. Patent Application No. 08/869,426; the claim to the benefit of Application No. 08/869,426 was withdrawn on October 16, 1998 during the prosecution of Application No. 09/089,377. Claims 1-16 have been canceled, and claims 17, 18, 19, 21, 22, 24, 28, 29, and 32 have been amended. A "markup" copy of the amended claims is found in Appendix 2. A "clean" copy of the amended and new claims is found in Appendix 3.

The amendments do not introduce new matter within the meaning of 35 U.S.C. §132. Canceled claims 1-16 were allowed, as amended, in U.S. Patent Application Serial No. 09/089,377. Claims 17, 18, 19, 21, 22, 24, 28, 29, and 32 have been amended to describe the inventive subject matter more clearly. Accordingly, the Examiner

is respectfully requested to enter the above amendments before examination.

The Examiner is welcomed to telephone the undersigned attorney if (s)he has any questions or comments.

Respectfully submitted,

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Appendix 1

Amendments to the Specification: clean copy (37 C.F.R. §1.121(b)(1)).

Please amend the specification by deleting the text at page 1, lines 4-7, and replacing it with the following:

"This application is a divisional of U.S. Patent Application No. 09/089,377, filed on June 3, 1998."

Appendix 2

Amendments to pending claims: mark-up copy (37 C.F.R. §1.121(c)(ii)).

Please cancel claims 1-16 without prejudice or disclaimer of the subject matter expressed therein.

Please amend claims 17, 18, 19, 21, 22, 24, 28, 29, and 32 as follows:

17. (Once amended) A pharmaceutical composition which comprises:

(i) an effective amount of a [heterocyclic ester or amide for treating alopecia or promoting hair growth in an animal; and] nitrogen-containing heterocyclic compound having two or more heteroatoms,

wherein said compound has a substituent -C(W)-C(Y)- which is attached to a nitrogen atom of the heterocyclic ring,

wherein W and Y are independently selected from the group consisting of O, S, CH_2, and H_2, and

wherein said compound is additionally substituted with a ester

or amide substituent attached to any atom of the heterocyclic ring other than said nitrogen atom,

provided that said ester or amide substituent is not an N-oxide of an ester or amide and further provided that said amide substituent is linked to the heterocyclic ring with a carbon-carbon bond; [and]

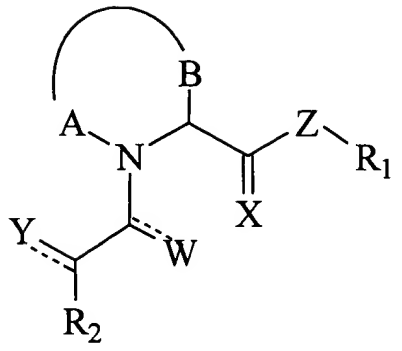
(ii) a second compound for treating alopecia or promoting hair growth; and

(iii) a pharmaceutical acceptable carrier.

18. (Once amended) The pharmaceutical composition of claim 17, wherein the [heterocyclic ester or amide] compound is non-immunosuppressive.

19. (Once amended) The pharmaceutical composition of claim 17, wherein the [heterocyclic ester or amide] compound has an affinity for an FKBP-type immunophilin.

21. (Once amended) The pharmaceutical composition of claim 17, wherein the [heterocyclic ester or amide is a] compound is of formula I



I

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A and B, together with the nitrogen and carbon atoms to which they are respectively attached, form a 5-7 membered saturated or unsaturated heterocyclic ring containing, in addition to the nitrogen atom, one or more additional O, S, SO, SO_2, N, NH, or NR_1 heteroatom;

X is O or S;

Z is O, NH, or NR_1;

W and Y are independently O, S, CH_2, or H_2;

R_1 is C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl, which is substituted with one or more substituent(s) independently selected from the group consisting of $(Ar_1)_n$, C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with $(Ar_1)_n$, C_3-C_8 cycloalkyl, C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with C_3-C_8 cycloalkyl, and Ar_2;

n is 1 or 2;

R_2 is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl or Ar_1,

wherein said alkyl, alkenyl, cycloalkyl or cycloalkenyl is either unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of C_1-C_4 straight or branched chain alkyl, C_2-C_4 straight or branched chain alkenyl, and hydroxy; and

A3

Ar_1 and Ar_2 are independently an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring,

wherein the ring is either unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy, benzyloxy, and amino[;],

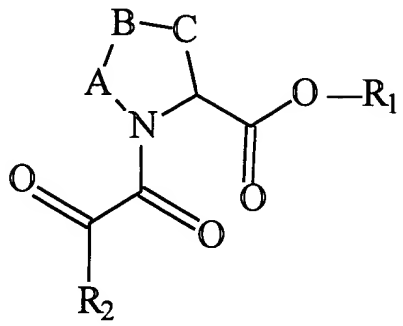
wherein the individual ring size is 5-6 members[;],

and wherein the heterocyclic ring [contains] <u>has</u> 1-6 heteroatom(s) independently selected from the group consisting of O, N, and S.

22. (Once amended) The pharmaceutical composition of claim 21, wherein [the mono- or bicyclic, carbo- or heterocyclic ring] <u>said Ar_1 or Ar_2</u> is selected from the group consisting of naphthyl,

indolyl, furyl, thiazolyl, thienyl, pyridyl, quinolinyl, isoquinolinyl, fluorenyl, and phenyl.

24. (Once amended) The pharmaceutical composition of claim 17, wherein the [heterocyclic ester or amide is a] compound is of formula II



II

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A, B and C are independently CH_2, O, S, SO, SO_2, NH, or NR_1, provided that A, B and C are not all CH_2;

R_1 is C_1-C_5 straight or branched chain alkyl or C_2-C_5 straight or branched chain alkenyl, which is substituted with one or more substituent(s) independently selected from the group consisting of $(Ar_1)_n$ and C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with $(Ar_1)_n$;

n is 1 or 2;

R_2 is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, or Ar_1; and

Ar_1 is a an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring,

wherein the ring is either unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy, benzyloxy, and amino[;],

wherein the individual ring size is 5-6 members[;],

and wherein the heterocyclic ring [contains] <u>has</u> 1-6 heteroatom(s) independently selected from the group consisting of O, N, and S.

A3

28. (Once amended) The pharmaceutical composition of claim 24, wherein the compound is selected from the group consisting of:

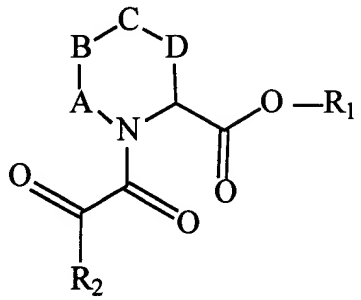
A4

3-phenyl-1-propyl(2*S*)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-(4-thiazolidine)carboxylate; <u>and</u>

3-(3-pyridyl)-1-propyl(2*S*)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-(4-thiazolidine) carboxylate; [and]

or a pharmaceutically acceptable salt[s], ester[s], [and] or solvate[s] thereof.

29. (Once amended) The pharmaceutical composition of claim 17, wherein the [heterocyclic ester or amide is a] compound is of formula III



III

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A, B, C and D are independently CH_2, O, S, SO, SO_2, NH, or NR_1, provided that A, B, C and D are not all CH_2;

R_1 is C_1-C_5 straight or branched chain alkyl or C_2-C_5 straight or branched chain alkenyl, which is substituted with one or more substituent(s) independently selected from the group consisting of $(Ar_1)_n$ and C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with $(Ar_1)_n$;

n is 1 or 2;

R_2 is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, or Ar_1; and

Ar_1 is an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring,

wherein the ring is either unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy, benzyloxy, and amino[;]

wherein the individual ring size is 5-6 members[;]

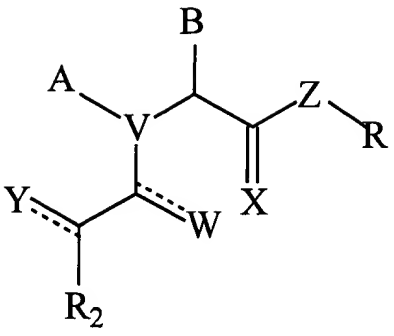
and wherein the heterocyclic ring [contains] has 1-6 heteroatom(s) independently selected from the group consisting of O, N, and S.

A4

32. (Once amended) [The pharmaceutical composition of claim 17, wherein the heterocyclic ester or amide is a] A pharmaceutical composition which comprises:

A5

(i) a compound of formula IV



IV

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

V is [C, N, or S] CH or N;

A and B, taken together with V and the carbon atom to which they are respectively attached, form a 5-7 membered saturated or unsaturated heterocyclic ring containing, in addition to V, one or more heteroatom(s) independently selected from the group consisting of O, S, SO, SO_2, N, NH, and NR;

R is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_9 cycloakyl, C_5-C_7 cycloalkenyl, or Ar_3,

wherein R is either unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of halo, haloalkyl, carbonyl, carboxy, hydroxy, nitro, trifluoromethyl, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy,

benzyloxy, thioalkyl, alkylthio, sulfhydryl, amino, alkylamino, aminoalkyl, aminocarboxyl, and Ar_4;

Ar_3 and Ar_4 are independently an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring;

wherein the individual ring size is 5-8 members[;],

wherein said heterocyclic ring [contains] has 1-6 heteroatom(s) independently selected from the group consisting of O, N, and S; [and

R_1, R_2, W, X, Y, and Z are as defined in claim 21 above.]

X is O or S;

Z is O, NH, or NR_1;

W and Y are independently O, S, CH_2, or H_2;

R_1 is C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl, which is substituted with one or more substituent(s) independently selected from the group consisting of $(Ar_1)_n$, C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with $(Ar_1)_n$, C_3-C_8 cycloalkyl, C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with C_3-C_8 cycloalkyl, and Ar_2;

n is 1 or 2; and

R_2 is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl or Ar_1.

wherein said alkyl, alkenyl, cycloalkyl or cycloalkenyl is either unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of C_1-C_4 straight or branched chain alkyl, C_2-C_4 straight or branched chain alkenyl, and hydroxy;

(ii) a second compound for treating alopecia or promoting hair growth; and

(iii) a pharmaceutically acceptable carrier.

Appendix 3

Ammendments to pending claims: clean copy (37 C.F.R. §1.121(c)(ii)).

17. (Once amended) A pharmaceutical composition which comprises:

(i) an effective amount of a nitrogen-containing heterocyclic compound having two or more heteroatoms,

wherein said compound has a substituent -C(W)-C(Y)- which is attached to a nitrogen atom of the heterocyclic ring,

wherein W and Y are independently selected from the group consisting of O, S, CH_2, and H_2, and

wherein said compound is additionally substituted with a ester or amide substituent attached to any atom of the heterocyclic ring other than said nitrogen atom,

provided that said ester or amide substituent is not an N-oxide of an ester or amide and further provided that said amide substituent is linked to the heterocyclic ring with a carbon-carbon bond;

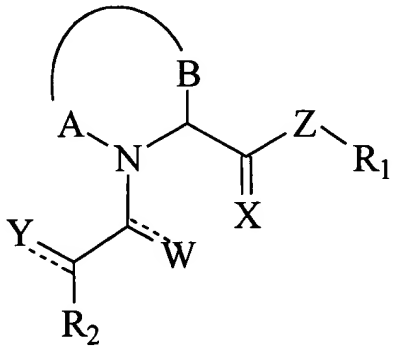
(ii) a second compound for treating alopecia or promoting hair growth; and

(iii) a pharmaceutically acceptable carrier.

18. (Once amended) The pharmaceutical composition of claim 17, wherein the compound is non-immunosuppressive.

19. (Once amended) The pharmaceutical composition of claim 17, wherein the compound has an affinity for an FKBP-type immunophilin.

21. (Once amended) The pharmaceutical composition of claim 17, wherein the compound is of formula I



I

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A and B, together with the nitrogen and carbon atoms to which they are respectively attached, form a 5-7 membered saturated or unsaturated heterocyclic ring containing, in addition to the nitrogen atom, one or more additional O, S, SO, SO_2, N, NH, or NR_1 heteroatom;

X is O or S;

Z is O, NH, or NR_1;

W and Y are independently O, S, CH_2, or H_2;

R_1 is C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl, which is substituted with one or more substituent(s) independently selected from the group consisting of $(Ar_1)_n$, C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with $(Ar_1)_n$, C_3-C_8 cycloalkyl, C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with C_3-C_8 cycloalkyl, and Ar_2;

n is 1 or 2;

R_2 is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl or Ar_1,

wherein said alkyl, alkenyl, cycloalkyl or cycloalkenyl is either unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of C_1-C_4 straight or branched chain alkyl, C_2-

C_4 straight or branched chain alkenyl, and hydroxy; and

Ar_1 and Ar_2 are independently an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring,

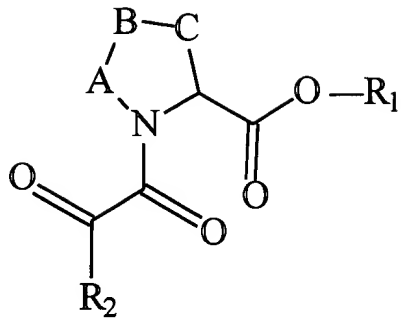
wherein the ring is either unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy, benzyloxy, and amino,

wherein the individual ring size is 5-6 members,

and wherein the heterocyclic ring has 1-6 heteroatom(s) independently selected from the group consisting of O, N, and S.

22. (Once amended) The pharmaceutical composition of claim 21, wherein said Ar_1 or Ar_2 is selected from the group consisting of naphthyl, indolyl, furyl, thiazolyl, thienyl, pyridyl, quinolinyl, isoquinolinyl, fluorenyl, and phenyl.

24. (Once amended) The pharmaceutical composition of claim 17, wherein the compound is of formula II



II

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A, B and C are independently CH_2, O, S, SO, SO_2, NH, or NR_1, provided that A, B and C are not all CH_2;

R_1 is C_1-C_5 straight or branched chain alkyl or C_2-C_5 straight or branched chain alkenyl, which is substituted with one or more substituent(s) independently selected from the group consisting of $(Ar_1)_n$ and C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with $(Ar_1)_n$;

n is 1 or 2;

R_2 is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, or Ar_1; and

Ar_1 is a an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring,

wherein the ring is either unsubstituted or substituted

with one or more substituent(s) independently selected from the group consisting of halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy, benzyloxy, and amino, wherein the individual ring size is 5-6 members, and wherein the heterocyclic ring has 1-6 heteroatom(s) independently selected from the group consisting of O, N, and S.

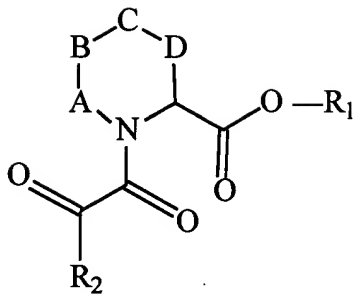
28. (Once amended) The pharmaceutical composition of claim 24, wherein the compound is selected from the group consisting of:

3-phenyl-1-propyl(2*S*)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-(4-thiazolidine)carboxylate; and

3-(3-pyridyl)-1-propyl(2*S*)-1-(3,3-dimethyl-1,2-dioxopentyl)-2-(4-thiazolidine) carboxylate;

or a pharmaceutically acceptable salt, ester, or solvate thereof.

29. (Once amended) The pharmaceutical composition of claim 17, wherein the compound is of formula III



III

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A, B, C and D are independently CH_2, O, S, SO, SO_2, NH, or NR_1, provided that A, B, C and D are not all CH_2;

R_1 is C_1-C_5 straight or branched chain alkyl or C_2-C_5 straight or branched chain alkenyl, which is substituted with one or more substituent(s) independently selected from the group consisting of $(Ar_1)_n$ and C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with $(Ar_1)_n$;

n is 1 or 2;

R_2 is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, or Ar_1; and

Ar_1 is an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring,

wherein the ring is either unsubstituted or substituted with one or more substituent(s) independently selected

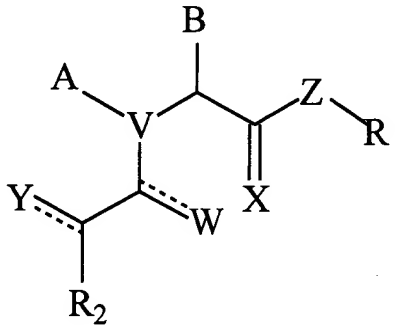
from the group consisting of halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy, benzyloxy, and amino,

wherein the individual ring size is 5-6 members,

and wherein the heterocyclic ring has 1-6 heteroatom(s) independently selected from the group consisting of O, N, and S.

32. (Once amended) A pharmaceutical composition which comprises:

(i) a compound of formula IV



IV

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

V is CH or N;

A and B, taken together with V and the carbon atom to which

they are respectively attached, form a 5-7 membered saturated or unsaturated heterocyclic ring containing, in addition to V, one or more heteroatom(s) independently selected from the group consisting of O, S, SO, SO_2, N, NH, and NR;

R is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_9 cycloakyl, C_5-C_7 cycloalkenyl, or Ar_3,

wherein R is either unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of halo, haloalkyl, carbonyl, carboxy, hydroxy, nitro, trifluoromethyl, C_1-C_6 straight or branched chain alkyl, C_2-C_6 straight or branched chain alkenyl, C_1-C_4 alkoxy, C_2-C_4 alkenyloxy, phenoxy, benzyloxy, thioalkyl, alkylthio, sulfhydryl, amino, alkylamino, aminoalkyl, aminocarboxyl, and Ar_4;

Ar_3 and Ar_4 are independently an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring;

wherein the individual ring size is 5-8 members,

wherein said heterocyclic ring has 1-6 heteroatom(s) independently selected from the group consisting of O, N, and S;

X is O or S;

Z is O, NH, or NR_1;

W and Y are independently O, S, CH_2, or H_2;

R_1 is C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl, which is substituted with one or more substituent(s) independently selected from the group consisting of $(Ar_1)_n$, C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with $(Ar_1)_n$, C_3-C_8 cycloalkyl, C_1-C_6 straight or branched chain alkyl or C_2-C_6 straight or branched chain alkenyl substituted with C_3-C_8 cycloalkyl, and Ar_2;

n is 1 or 2; and

R_2 is either C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl or Ar_1,

wherein said alkyl, alkenyl, cycloalkyl or cycloalkenyl is either unsubstituted or substituted with one or more substituent(s) independently selected from the group consisting of C_1-C_4 straight or branched chain alkyl, C_2-C_4 straight or branched chain alkenyl, and hydroxy;

(ii) a second compound for treating alopecia or promoting hair growth; and

(iii) a pharmaceutically acceptable carrier.